

REVISED SPECIFICATION

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Needs remain for compositions and methods for improved means for evaluating *the in vivo* activity and/or efficacy of these morphogenic proteins and analogs thereof. It is anticipated that different morphogens will have differing specific activities for effecting morphogenesis in a given tissue or organ. It further is anticipated that analogs of morphogens, including candidate non-protein-based “small molecule” functional mimetics, will need to be evaluated for their ability to functionally substitute for a given morphogen *in vivo*. It further is anticipated that, for a given indication, such as treating an embolic stroke, for example, dosing and routes of administration can vary depending on the individual’s overall health, age and condition. Thus, needs also remain for evaluating the pharmacokinetics of a morphogenic protein or analog thereof, including evaluating dosing, preferred administration times, and preferred administration routes for administering a given morphogen, and/or analog to a given individual, for different therapeutic applications.

Accordingly, it is an object of the instant invention to provide formulations and methods of use thereof for quickly evaluating the *in vivo* activity of morphogens and/or analogs thereof.

These and other objects, along with advantages and features of the invention disclosed herein, will be apparent from the description, drawings and claims that follow.

Summary of the Invention

The present invention is based on the discovery that a true tissue morphogen such as OP-1 provided systemically, alone in its mature dimeric form, or as part of a soluble complex, can induce new replacement tissue regeneration at a localized, permissive defect site distal to the site of administration. Specifically, systemically administered protein is sufficient to induce formation of new functional replacement tissue, sufficient to repair a local defect in a tissue,

including skeletal or orthopedic tissues, liver, pancreas, lung, cardiac, renal, uterine, intestinal gastrointestinal tissue. (As used herein, “orthopedic” or “skeletal” or “joint” or “chondrogenic” tissue is understood to encompass the skeletal and skeletal joint tissues: bone, cartilage, tendon, ligament, and synovial membrane tissues.) It further has been discovered that a single injection of morphogenic protein is sufficient to induce the desired biological effect, and that administration is not time-sensitive, provided mesenchymal progenitor cells are accessible to the defect site. That is, morphogenic protein can be provided to an individual having a local